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Allergic reactions after ingestion of erythritol-containing foods and beverages

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To The editor

Erythritol (ERT; 1,2,3,4-butanetetrol) is a 4-carbon sugar alcohol prepared from glucose by fermentation,1 ERT occurs naturally in certain foods (mushroom, watermelon, pear, grape, wine, beer, soy sauce, cheese) at levels up to 0.13%. ERT is used to sweeten beverages and snack foods in Japan, where more than 125 million people consume more than 5 billion servings of ERT-sweetened foods annually. Anecdotal and unconfirmed reports of adverse reactions to ERT-containing products (estimated prevalence, <1 per million people) have appeared.2 To clarify the pathophysiology of these reactions, we studied 2 Japanese volunteers who had experienced multiple reactions to ERT-containing foods.

A 28-year-old woman developed generalized urticaria after eating various ERT-containing foods. Results of puncture skin tests with more than 40 lots of ERT (100 mg/mL in 50% glycerine) from 3 different manufacturers were negative, but results of intradermal (ID) titration skin tests with ERT solutions in saline solution were positive, with endpoints between 4 and 20 mg/mL. Results of ID skin tests with ERT (100 mg/mL) in 7 healthy control subjects were negative. This first volunteer's peripheral blood leukocytes released <8% total histamine when challenged in vitro with serial dilutions of ERT. However, she experienced facial swelling and urticaria after separate single-blinded, graded oral challenge tests with 2 lots of ERT (cumulative dose, 1.6 g). She tolerated a control oral challenge with sucrose (cumulative dose, 16.6 g). Serum levels of tryptase, C3, C4, and total hemolytic complement measured 1 hour after the 2 ERT challenges were unchanged from baseline values.

A 50-year-old man experienced 3 episodes of generalized urticaria, 2 of which included physician-documented hypotension (systolic BP readings, 90 and 74) after eating ERT-containing foods. Results of specific IgE antibody assays to 18 foods were negative. Known to be sensitized to house dust mite, this second volunteer exhibited positive puncture skin test results with all lots (>40) of ERT tested (100 mg/mL in 50% glycerine), whereas

results of control tests with glyceraldehyde, erythrose, erythrulose, glycerol, and various other polyols (xylitol, mannitol, sorbitol, maltitol, and isomalt, containing 5, 6, 6, 12, and 12 carbons, respectively—all at 100 mg/mL) were negative. ID skin test titrations with multiple lots of fermentation-derived ERT, as well as ERT synthesized through use of a nonfermentation procedure,3 all produced positive reactions with endpoints between 160 µg/mL and 1 mg/mL. Results of ID skin tests with synthetic ERT (100 mg/mL in 7 healthy control subjects were negative. The volunteer's peripheral blood leukocytes were challenged with ERT and xylitol in the presence or absence of 20% autologous serum. Without autologous serum, significant histamine release (>10%) was obtained only with mite extract and anti-IgE. However, in the presence of 20% autologous serum, small amounts of histamine were released in a dose-dependent manner with both synthetic ERT (maximum release, 17%) and fermentation-derived ERT (maximum release, 23%). No histamine release was observed with xylitol. The volunteer refused oral challenge feedings because of the severity of his prior systemic reactions.

The positive ID skin test result with synthetic ERT in the second volunteer strongly suggests that it is the ERT itself, not a co-purifying contaminant, that is responsible for the reactions. We reproduced signs and symptoms of a generalized allergic reaction in the first volunteer by single-blinded oral challenge testing with 2 lots of fermentation-derived ERT from different manufacturers. No objective evidence of mast cell activation was noted in blood samples obtained within 1 hour of the positive oral challenge reactions, perhaps because of the mild but definite symptoms elicited. Collectively, these data suggest that ERT might function as an allergen or hapten to mediate IgE-dependent anaphylactic reactions. Alternatively, a non–IgE-mediated mechanism of tissue mast cell or blood leukocyte activation might be operative. The pathophysiologic mechanisms underlying these reactions remain obscure.

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References

1.Munro IC, Berndt WO, Borzelleca JF, Flamm G, Lynch BS, Kennepohl E, et al. Erythritol: an interpretive summary of biochemical, metabolic, toxicological, and clinical data. Food Chem Toxicol. 1998;36:1139–1174
View In ArticleMEDLINECrossRef
2.Hino H, Kasai S, Hattori N, Kenjo K. A case of allergic urticaria caused by erythritol. J Dermatol. 2000;27:163–165
View In ArticleMEDLINE
3.US patent EP 0 767 159 Al, April 1997.
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